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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/291,347	04/14/1999	JULIAN ALEXIS JOHN HANAK	CACO-0051	1979

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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 01/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/291,347	HANAK ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on th cover she t with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-14,38-43 and 45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *13,14,40-42 and 45* is/are allowed.

6)☒ Claim(s) *7-12,38,39 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 7-14, 38-43, and 45 are pending.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/2/2003 has been entered.

Applicant's amendment of claims 7-14, 43, addition of claim 45, and cancellation of claim 44 in a communication filed on 10/2/2003 are acknowledged.

The Examiner contacted Applicant's representative on 1/7/2004 but no agreement could be reached to place the application in condition for allowance.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112, First Paragraph

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 7-12, 38-39 and 43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of preparing RNA-free cellular components by overexpressing RNases (either constitutively or inducibly) in the periplasm of a microbial cell to degrade substantially all of the RNA present, does not reasonably provide enablement for a method of preparing RNA-free cellular components by overexpressing RNases (either constitutively or inducibly) in the cytoplasm of a microbial cell to degrade substantially all of the RNA present.. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

Claims 7-12, 38-39 and 43 are directed to a method of preparing RNA-free cellular components by overexpressing a genus of RNases (either constitutively or inducibly) in the cytoplasm of a microbial cell to degrade substantially all of the RNA present. While the specification discloses a method of preparing RNA-free cellular components by overexpressing RNases in the periplasm of a microbial cell to degrade RNA, the specification fails to disclose a method of preparing RNA-free cellular components by overexpressing RNases in the cytoplasm of a microbial cell to degrade substantially all of the RNA present. As indicated in the Advisory Action mailed 6/3/2003 and the interview of 9/16/2003, Zhu et al. teaches that while overexpression of RNase I was intended to occur in the cytoplasm (E. coli), 85% of the RNase activity was found in the periplasm and the remaining RNase found in the cytoplasm was most likely inactive. Therefore, in the absence of experimental evidence showing that overexpression of any RNase in the cytoplasm would result in RNase activity sufficient to degrade substantially all of the RNA present, as required by the claims, and taking into consideration the teachings of the prior art regarding the lack of RNase activity when overexpression occurs in the cytoplasm, one cannot reasonably conclude that the claimed invention is enabled by the teachings of the specification.

3. Applicants submit that the teachings of Meador et al. (Eur J Biochem 187:549-553, 1990; cited by the previous Examiner of record) is experimental evidence which contradicts the teachings of Zhu et al. that RNase in the cytoplasm is not active. Applicants also submit references by Cannistraro et al. (Eur

J Biochem 181:363-370, 1989) and Meador et al. (Gene 95:1-7, 1990) in support of the argument that the teachings of Meador et al. (Eur J Biochem 187:549-553, 1990) contradict the teachings of Zhu et al.

4. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejection. While it is agreed that the references submitted by Applicants indicate that RNase M is active in the cytoplasm, it is noted that it is not the Examiner's contention that Zhu et al. teaches that no RNase (of any type) is active in the cytoplasm. One of skill in the art would expect certain RNases, expressed at normal levels, to be active in the cytoplasm to degrade mRNA which is no longer needed. As indicated above, Zhu et al. teaches that overexpression (higher than normal expression levels) of RNase I in the cytoplasm results in most of the active RNase to be found in the periplasm and the RNase found in the cytoplasm is mostly inactive. As such, there is some experimental evidence which suggests that overexpression of an RNase which is intended to occur in the cytoplasm (i.e. no secretion signal) results in very little active RNase in the cytoplasm and most of the RNase activity to be found in the periplasm. The teachings of Meador et al. (Eur J Biochem 187:549-553, 1990), Cannistraro et al. (Eur J Biochem 181:363-370, 1989), and Meador et al. (Gene 95:1-7, 1990) refer to RNase M as an RNase which, when expressed at wild-type levels, is active in the cytoplasm of E. coli. None of these references teaches that overexpression of the RNase in E. coli, (i.e. higher than normal expression levels), results in active RNase in the cytoplasm, which is required in the claimed method in order to degrade substantially all of the RNA present. Therefore, for the reasons set forth above, one cannot reasonably conclude that the specification provides sufficient guidance to enable one of skill in the art to practice the invention in a manner reasonably correlated with the scope of the claims.

Allowable Subject Matter

5. Claims 13-14, 40-42 and 45 appear to be allowable over the prior art of record.

Conclusion

6. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600